

Application No. 10/038,591

Filed: January 4, 2002

Title: ANTIBODIES TO INSULIN-LIKE GROWTH FACTOR I RECEPTOR

Confirmation No.: 1445

1-19. (Cancelled)

20. (Cancelled)

21-22. (Cancelled)

~~84~~ 23. (Currently amended) A method of detecting the presence or location of an IGF-IR-expressing tumor in a subject in need thereof, comprising the steps of:

a) administering the antibody or antigen-binding portion according to claim ~~34~~ or an antibody according to claim ~~39~~ or ~~46~~ to the subject; and

b) detecting binding of said antibody,

wherein said binding indicates the presence or location of the tumor.

~~85~~ 24. (Currently amended) A method of treating cancer in a human patient wherein said patient overexpresses IGF-I or IGF-IR, comprising the step of administering to the human patient an amount of the antibody or antigen-binding portion according to claim ~~34~~ effective to treat said cancer.

~~86~~ 25. (Currently amended) A method of treating a patient in need thereof, wherein said patient overexpresses IGF-I or IGF-IR, with the antibody or antigen-binding portion thereof according to claim ~~34~~, comprising the step of administering to the patient an effective amount of the antibody.

~~85~~ ~~87~~ 26. (Currently amended) The method according to either of claims claim 24 or 25, further comprising the step of administering an anti-neoplastic, anti-tumor, anti-angiogenic or chemotherapeutic agent.

27. (Cancelled)

28. (Cancelled)

29. (Cancelled)

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30. (Cancelled)

31. (Cancelled)

32. (Cancelled)

33. (Cancelled)

34. (Currently amended) A ~~human~~ monoclonal antibody that specifically binds ~~human~~ insulin-like growth factor I receptor (IGF-IR) or an antigen-binding portion of said antibody, wherein the antibody or portion comprises the amino acid sequences of the CDR1, CDR2 and CDR3 regions found in a variable domain selected from the group consisting of:

(a) the variable domain of the light chain of antibody 2.13.2;

and

(b) the variable domain of a light chain comprising the amino acid sequence in SEQ ID NO: 6;

~~— (c) — the variable domain of the heavy chain of antibody 2.13.2;~~

~~— (d) — the variable domain of a heavy chain comprising the amino acid sequence in SEQ ID NO: 8; and~~

~~— (e) — the variable domain of a light chain comprising SEQ ID NO: 6 and the variable domain of a heavy chain comprising SEQ ID NO: 8.~~

2 35. (Currently amended) The ~~human~~ monoclonal antibody or antigen-binding portion according to claim 34, further comprising the amino acid sequences of the heavy chain CDRs of antibody 2.13.2 and light chain CDRs of antibody 2.13.2.

3 36. (Currently amended) A monoclonal antibody or an antigen binding portion thereof that specifically binds ~~human~~ insulin-like growth factor I receptor (IGF-IR), wherein said antibody comprises a ~~variable domain of a  $\kappa$  light chain, and wherein~~

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~~said variable domain of a  $\kappa$  light chain comprises the amino acid sequence in SEQ ID NO: 6.~~

4 37. (Currently amended) A monoclonal antibody or an antigen-binding portion thereof that specifically binds human insulin like growth factor I receptor (IGF-IR), wherein said antibody comprises ~~a variable domain of a heavy chain, and wherein said variable domain of a heavy chain comprises the amino acid sequence in SEQ ID NO: 8.~~

5 38. (Currently amended) The monoclonal antibody or antigen-binding portion according to claim 37, wherein said antibody further comprises ~~a variable domain of a light chain, and wherein said variable domain of a light chain comprises the amino acid sequence in SEQ ID NO: 6.~~

6 39. (Currently amended) A monoclonal antibody that specifically binds human insulin-like growth factor I receptor (IGF-IR), wherein said antibody comprises the amino acid sequence of the heavy chain sequence within SEQ ID NO: 45, without the signal sequence, and the amino acid sequence of the light chain sequence within SEQ ID NO: 47, without the signal sequence.

7 40. (Currently amended) A monoclonal antibody or an antigen-binding portion thereof that specifically binds human IGF-IR, comprising ~~heavy chain CDR1, CDR2 and CDR3 regions, said CDR regions comprising the CDR1, CDR2 and CDR3 amino acid sequences, respectively, in SEQ ID NO:45.~~

8 41. (Currently amended) The monoclonal antibody or antigen-binding portion according to claim 40, ~~wherein said heavy chain further comprises~~ comprising the framework amino acid sequences in SEQ ID NO: 45.

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9 ~~42~~. (Currently amended) A monoclonal antibody that specifically binds ~~human~~ IGF-IR comprising the amino acid sequence of SEQ ID NO: 45, without the signal sequence, or an antigen-binding portion of said antibody.

10 ~~43~~. (Currently amended) A monoclonal antibody or an antigen binding portion thereof that specifically binds ~~human~~ IGF-IR, comprising ~~light chain CDR1, CDR2 and CDR3 regions, said CDR regions comprising~~ the CDR1, CDR2 and CDR3 amino acid sequences, respectively, in SEQ ID NO: 47.

11 ~~44~~. (Currently amended) The monoclonal antibody or antigen-binding portion according to claim ~~43~~, wherein said ~~light chain~~ further ~~comprises~~comprising the framework amino acid sequences in SEQ ID NO: 47.

12 ~~45~~. (Currently amended) A monoclonal antibody that specifically binds ~~human~~ IGF-IR comprising the amino acid sequence in SEQ ID NO: 47, without the signal sequence, or an antigen-binding portion of said antibody.

13 ~~46~~. (Currently amended) A monoclonal antibody that specifically binds ~~human~~ insulin-like growth factor I receptor (IGF-IR) wherein the heavy chain amino acid sequence is SEQ ID NO: 45, without the signal sequence, and the light chain amino acid sequence is SEQ ID NO: 47, without the signal sequence.

14 ~~47~~. (Previously presented) A hybridoma cell line having American Type Culture Collection (ATCC) accession number PTA-2788.

15 ~~48~~. (Currently amended) A monoclonal antibody or an antigen-binding portion thereof, that specifically binds ~~human~~ IGF-IR, comprising the heavy chain variable domain and the light chain variable domain of the antibody produced by the hybridoma cell line of claim ~~47~~.

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<sup>16</sup> ~~49~~ (Previously presented) The monoclonal antibody produced by the hybridoma cell line of claim <sup>14</sup> ~~47~~.

<sup>17</sup> ~~50~~ (Currently amended) A monoclonal antibody that specifically binds ~~human~~ IGF-IR comprising the heavy chain amino acid sequence and the light chain amino acid sequence of the antibody produced by the hybridoma cell line having ATCC accession number PTA-2788.

<sup>18</sup> ~~51~~ (Currently amended) A monoclonal antibody that specifically binds ~~human~~ IGF-IR comprising the amino acid sequence of the heavy chain and the amino acid sequence of the light chain of antibody 2.13.2.

<sup>18</sup> ~~51~~ <sup>19</sup> ~~52~~ (Previously presented) The monoclonal antibody according to claim ~~51~~, wherein the antibody is monoclonal antibody 2.13.2.

53. (Cancelled)

<sup>20</sup> ~~54~~ (Currently amended) A monoclonal antibody or antigen-binding portion thereof that specifically binds ~~human~~ IGF-IR, comprising a heavy chain amino acid sequence that utilizes ~~the~~ human V<sub>H</sub>3-23 gene.

55. (Cancelled)

<sup>21</sup> ~~56~~ (Currently amended) A monoclonal antibody or antigen-binding portion thereof that specifically binds ~~human~~ IGF-IR, comprising a light chain amino acid sequence that utilizes the human V<sub>κ</sub> A30 gene.

<sup>22</sup> ~~57~~ (Currently amended) The ~~human~~ monoclonal antibody or antigen-binding portion according to claim <sup>1</sup> ~~34~~, wherein said antibody is selected from the group consisting of: an immunoglobulin G (IgG), an IgM, an IgE, an IgA or an IgD molecule, a single chain antibody or a bispecific antibody.

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1 23 58. (Previously presented) The antigen-binding portion according to claim 34, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

2 24 59. (Previously presented) The antigen-binding portion according to claim 35, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

3 25 60. (Previously presented) The antigen-binding portion according to claim 36, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

4 26 61. (Previously presented) The antigen-binding portion according to claim 37, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

5 27 62. (Previously presented) The antigen-binding portion according to claim 38, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

7 28 63. (Previously presented) The antigen-binding portion according to claim 40, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

8 29 64. (Previously presented) The antigen-binding portion according to claim 41, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

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9 306<sup>5</sup>. (Previously presented) The antigen-binding portion according to claim 42, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

10 316<sup>6</sup>. (Previously presented) The antigen-binding portion according to claim 43, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

11 326<sup>7</sup>. (Previously presented) The antigen-binding portion according to claim 44, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

12 336<sup>8</sup>. (Previously presented) The antigen-binding portion according to claim 45, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

15 346<sup>9</sup>. (Previously presented) The antigen-binding portion according to claim 46, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

20 357<sup>10</sup>. (Previously presented) The antigen-binding portion according to claim 47, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

21 367<sup>11</sup>. (Previously presented) The antigen-binding portion according to claim 48, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

22 377<sup>12</sup>. (Previously presented) The antigen-binding portion according to claim 49, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

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38<sup>1</sup>/<sub>3</sub>. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 34 and a pharmaceutically acceptable carrier.

39<sup>1</sup>/<sub>4</sub>. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 35 and a pharmaceutically acceptable carrier.

40<sup>1</sup>/<sub>5</sub>. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 36 and a pharmaceutically acceptable carrier.

41<sup>1</sup>/<sub>6</sub>. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 37 and a pharmaceutically acceptable carrier.

42<sup>1</sup>/<sub>7</sub>. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 38 and a pharmaceutically acceptable carrier.

43<sup>1</sup>/<sub>8</sub>. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 39 and a pharmaceutically acceptable carrier.

44<sup>1</sup>/<sub>9</sub>. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 40 and a pharmaceutically acceptable carrier.



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<sup>45</sup>80. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim <sup>9</sup>42 and a pharmaceutically acceptable carrier.

<sup>46</sup>81. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim <sup>10</sup>43 and a pharmaceutically acceptable carrier.

<sup>47</sup>82. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim <sup>11</sup>44 and a pharmaceutically acceptable carrier.

<sup>48</sup>83. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim <sup>12</sup>45 and a pharmaceutically acceptable carrier.

<sup>49</sup>84. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim <sup>13</sup>46 and a pharmaceutically acceptable carrier.

<sup>50</sup>85. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim <sup>20</sup>47 and a pharmaceutically acceptable carrier.

<sup>51</sup>86. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim <sup>21</sup>48 and a pharmaceutically acceptable carrier.

<sup>52</sup>87. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim <sup>22</sup>49 and a pharmaceutically acceptable carrier.

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53 88. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 39 and a pharmaceutically acceptable carrier.

54 89. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 46 and a pharmaceutically acceptable carrier.

55 90. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 49 and a pharmaceutically acceptable carrier.

56 91. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 50 and a pharmaceutically acceptable carrier.

57 92. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 51 and a pharmaceutically acceptable carrier.

58 93. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 52 and a pharmaceutically acceptable carrier.

94. (Cancelled)

59 95. (Previously presented) A pharmaceutical composition comprising the monoclonal antibody according to claim 54 and a pharmaceutically acceptable carrier.

96. (Cancelled)

60 97. (Previously presented) The pharmaceutical composition according to claim 73, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

61 98. (Previously presented) The pharmaceutical composition according to claim 74, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

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<sup>40</sup> 62 99. (Previously presented) The pharmaceutical composition according to claim <sup>75</sup> 75, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>41</sup> 63 100. (Previously presented) The pharmaceutical composition according to claim <sup>76</sup> 76, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>42</sup> 64 101. (Previously presented) The pharmaceutical composition according to claim <sup>77</sup> 77, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>43</sup> 65 102. (Previously presented) The pharmaceutical composition according to claim <sup>78</sup> 78, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>44</sup> 66 103. (Previously presented) The pharmaceutical composition according to claim <sup>79</sup> 79, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>45</sup> 67 104. (Previously presented) The pharmaceutical composition according to claim <sup>80</sup> 80, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>46</sup> 68 105. (Previously presented) The pharmaceutical composition according to claim <sup>81</sup> 81, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>47</sup> 69 106. (Previously presented) The pharmaceutical composition according to claim <sup>82</sup> 82, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>48</sup> 70 107. (Previously presented) The pharmaceutical composition according to claim <sup>83</sup> 83, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>49</sup> 71 108. (Previously presented) The pharmaceutical composition according to claim <sup>84</sup> 84, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

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<sup>72</sup> 109. (Previously presented) The pharmaceutical composition according to claim <sup>85</sup> 85, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>73</sup> 110. (Previously presented) The pharmaceutical composition according to claim <sup>86</sup> 86, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>74</sup> 111. (Previously presented) The pharmaceutical composition according to claim <sup>87</sup> 87, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>75</sup> 112. (Previously presented) The pharmaceutical composition according to claim <sup>88</sup> 88, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>76</sup> 113. (Previously presented) The pharmaceutical composition according to claim <sup>89</sup> 89, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>77</sup> 114. (Previously presented) The pharmaceutical composition according to claim <sup>90</sup> 90, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>78</sup> 115. (Previously presented) The pharmaceutical composition according to claim <sup>91</sup> 91, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>79</sup> 116. (Previously presented) The pharmaceutical composition according to claim <sup>92</sup> 92, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>80</sup> 117. (Previously presented) The pharmaceutical composition according to claim <sup>93</sup> 93, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

118. (Cancelled)

<sup>81</sup> 119. (Previously presented) The pharmaceutical composition according to claim <sup>94</sup> 94, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

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~~80~~ 120. (Previously presented) An isolated cell line that produces the antibody according to claim ~~1~~<sup>1</sup>/<sub>4</sub>.

~~83~~ 121. (Previously presented) The cell line according to claim ~~1~~<sup>82</sup>/<sub>20</sub> that produces antibody 2.13.2, or an antibody comprising the amino acid sequences of antibody 2.13.2.

~~88~~ 122. (Currently amended) A method for decreasing IGF-IR activation in a subject in need thereof comprising the step of administering to the subject an anti-IGF-IR antibody or ~~antigen-binding portion~~ according to claim ~~3~~<sup>6</sup>/<sub>934</sub>.

~~89~~ 123. (Currently amended) A method for increasing IGF-IR associated tyrosine phosphorylation in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody or antigen-binding portion according to claim ~~3~~<sup>6</sup>/<sub>934</sub>.

~~90~~ 124. (Currently amended) A method for decreasing IGF-IR signaling in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody or ~~antigen-binding portion~~ according to claim ~~3~~<sup>6</sup>/<sub>934</sub>.

~~91~~ 125. (Currently amended) A method for decreasing IGF-IR binding to IGF-I or IGF-II in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody or ~~antigen-binding portion~~ according to claim ~~3~~<sup>6</sup>/<sub>934</sub>.

~~92~~ 126. (Currently amended) A method for decreasing the level of IGF-IR in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody or antigen-binding portion according to claim ~~3~~<sup>6</sup>/<sub>934</sub>.

~~93~~ 127. (Currently amended) A method for inhibiting tumor growth in a subject in need thereof wherein said subject overexpresses IGF-I or IGF-IR, comprising

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the step of administering to the subject an anti-IGF-IR antibody or antigen-binding portion according to claim <sup>61</sup>3934.

<sup>94</sup> 128. (Previously presented) The method according to claim <sup>93</sup>127, wherein the tumor is a colorectal tumor.

<sup>95</sup> 129. (Previously presented) The method according to claim <sup>93</sup>127, wherein the tumor is a breast cancer tumor.

<sup>96</sup> 130. (Previously presented) The method according to claim <sup>93</sup>127, wherein the tumor is an epidermoid carcinoma cell tumor.

<sup>97</sup> 131. (Previously presented) The method according to claim <sup>87</sup>126, wherein the anti-neoplastic agent is adriamycin.

<sup>98</sup> 132. (Currently amended) A method of detecting the presence or location of an IGF-IR-expressing tumor in a subject in need thereof, comprising the steps of: <sup>6</sup>

(a) administering the antibody according to any one of claims <sup>13</sup>39, <sup>18</sup>or <sup>46</sup>46 or <sup>51</sup>51; and

(b) detecting binding of said antibody, determining the expression of IGF-IR in the subject by localizing where the antibody has bound; and

(c) diagnosing the presence or location of the tumor wherein said binding indicates the presence or [a] location of the tumor.

<sup>99</sup> 133. (Currently amended) A method of treating cancer in a human patient wherein said patient overexpresses IGF-I or IGF-IR, comprising the step of administering to the human patient an amount of the antibody according to claim <sup>61</sup>39 or <sup>13</sup>46 effective to treat said cancer.

<sup>100</sup> 134. (Currently amended) A method of treating a patient in need thereof with the antibody according to claim <sup>6</sup>39, or <sup>13</sup>46 or <sup>18</sup>51, wherein said patient overexpresses

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IGF-I or IGF-IR comprising the step of administering to the patient an effective amount of the antibody.

<sup>100</sup> 101 <sup>135</sup> 135. (Currently amended) The method according to either of claims <sup>99</sup> 133 or <sup>134</sup> 134, further comprising the step of administering an anti-neoplastic, anti-tumor, anti-angiogenic or chemotherapeutic agent.

<sup>102</sup> 136. (Previously presented) A method for decreasing IGF-IR activation in a subject in need thereof comprising the step of administering to the subject an anti-IGF-IR antibody according to claim <sup>6</sup> 39 or <sup>13</sup> 46.

<sup>103</sup> 137. (Previously presented) A method for increasing IGF-IR associated tyrosine phosphorylation in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody according to claim <sup>6</sup> 39 or <sup>13</sup> 46.

<sup>104</sup> 138. (Previously presented) A method for decreasing IGF-IR signaling in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody according to claim <sup>6</sup> 39 or <sup>13</sup> 46.

<sup>105</sup> 139. (Previously presented) A method for decreasing IGF-IR binding to IGF-I or IGF-II in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody according to claim <sup>6</sup> 39 or <sup>13</sup> 46.

<sup>106</sup> 140. (Previously presented) A method for decreasing the level of IGF-IR in a subject in need thereof, comprising the step of administering to the subject an anti-IGF-IR antibody according to claim <sup>6</sup> 39 or <sup>13</sup> 46.

<sup>107</sup> 141. (Currently amended) A method for inhibiting tumor growth in a subject in need thereof wherein said subject overexpresses IGF-I or IGF-IR, comprising the step of administering to the subject an anti-IGF-IR antibody according to claim <sup>6</sup> 39 or <sup>13</sup> 46.<sup>13</sup>

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<sup>108</sup>142. (Previously presented) The method according to claim <sup>107</sup>141, wherein the tumor is a colorectal tumor.

<sup>109</sup>143. (Previously presented) The method according to claim <sup>107</sup>141, wherein the tumor is a breast cancer tumor.

<sup>110</sup>144. (Previously presented) The method according to claim <sup>107</sup>141, wherein the tumor is an epidermoid carcinoma cell tumor.

<sup>111</sup>145. (Previously presented) The method according to claim <sup>101</sup>145, wherein the anti-neoplastic agent is adriamycin.

146. (Cancelled)

147. (Cancelled)

148. (Cancelled)

149. (Cancelled)

150. (Cancelled)

<sup>112</sup>151. (New) A monoclonal antibody that specifically binds insulin-like growth factor I receptor (IGF-IR) or an antigen-binding portion of said antibody, wherein the antibody or portion comprises the amino acid sequences of the CDR1, CDR2 and CDR3 regions found in a heavy chain variable domain selected from the group consisting of:

(a) the variable domain of the heavy chain of antibody 2.13.2;

and



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(b) the variable domain of a heavy chain comprising the amino acid sequence in SEQ ID NO: 8.

<sup>112</sup>  
113 ~~152~~. (New) The monoclonal antibody or antigen-binding portion according to claim ~~151~~<sup>112</sup>, wherein said antibody is selected from the group consisting of: an immunoglobulin G (IgG), an IgM, an IgE, an IgA or an IgD molecule, a single chain antibody or a bispecific antibody.

<sup>112</sup>  
114 ~~153~~. (New) The antigen-binding portion according to claim ~~151~~<sup>112</sup>, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

<sup>112</sup>  
115 ~~154~~. (New) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim ~~151~~<sup>112</sup> and a pharmaceutically acceptable carrier.

<sup>112</sup>  
116 ~~155~~. (New) The pharmaceutical composition according to claim ~~151~~<sup>112</sup>, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

<sup>112</sup>  
117 ~~156~~. (New) An isolated cell line that produces the antibody according to claim ~~151~~<sup>112</sup>.

<sup>112</sup>  
118 ~~157~~. (New) The monoclonal antibody or antigen-binding portion thereof according to claim ~~154~~<sup>112</sup>, wherein the heavy chain amino acid sequence further utilizes a human D6-19 gene and a human JH6 gene.

<sup>112</sup>  
119 ~~158~~. (New) The monoclonal antibody or antigen-binding portion according to claim ~~156~~<sup>112</sup>, wherein the light chain amino acid sequence further utilizes a human Jk1 gene.

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120 159. (New) A method of detecting the presence or location of an IGF-IR expressing tumor in a subject, comprising the steps of:

- a) administering the antibody according to claim 21/160 to the subject; and
- b) detecting binding of said antibody, wherein said binding indicates the presence or location of the tumor.

121 160. (New) A monoclonal antibody that specifically binds insulin-like growth factor I receptor (IGF-IR) or an antigen-binding portion of said antibody, wherein the antibody or portion comprises the amino acid sequences of the CDR1, CDR2 and CDR3 regions found in the variable domain of a light chain comprising SEQ ID NO: 6 and the amino acid sequences of the CDR1, CDR2 and CDR3 regions found in the variable domain of a heavy chain comprising SEQ ID NO: 8.

122 161. (New) The monoclonal antibody or antigen-binding portion according to claim 121/160, wherein said antibody is selected from the group consisting of: an immunoglobulin G (IgG), an IgM, an IgE, an IgA or an IgD molecule, a single chain antibody or a bispecific antibody.

123 162. (New) The antigen-binding portion according to claim 121/160, wherein said portion is selected from the group consisting of: a Fab fragment, an F(ab')<sub>2</sub> fragment and an Fv fragment.

124 163. (New) A pharmaceutical composition comprising the monoclonal antibody or antigen-binding portion according to claim 121/160 and a pharmaceutically acceptable carrier.

125 164. (New) The pharmaceutical composition according to claim 121/160, further comprising an antineoplastic, chemotherapeutic or anti-tumor agent.

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12/126 165. (New) An isolated cell line that produces the antibody according to claim 160.

127 166. (New) The method according to claim 85/24, further comprising the step of administering at least one additional chemotherapeutic agent.

128 167. (New) The method according to claim 85/24, wherein said method further comprises radiotherapy.

129 168. (New) The method according to claim 99/163, further comprising the step of administering at least one additional chemotherapeutic agent.

130 169. (New) The method according to claim 99/133, wherein said method further comprises radiotherapy.